Amendments to the Specification:

Please replace the paragraph beginning at page 6, line 18, with the following:

--Figure 3 shows a reaction scheme for the coupling of the cyclosporin A derivative to a biotin-labeled peptide (SEQ ID NOS:83-85).--

Please replace the paragraph beginning at page 6, line 20, with the following:

--Figure 4 shows a reaction scheme for coupling of a cyclosporin A derivative to an unlabeled peptide (SEQ ID NO:7).--

Please replace the paragraph beginning at page 7, line 7, with the following:

--Figure 6 displays a synthetic scheme for a chemical conjugate between a heptamer of L-arginine (SEQ ID NO:3) and cyclosporin A (panel A) and its pH dependent chemical release (SEQ ID NO:6) (panel B). The α-chloro ester (6i) was treated with benzylamine in the presence of sodium iodide to effect substitution, giving the secondary amine (6ii). Amine (6ii) was treated with anhydride (6) and the resultant crude acid (6iii) was converted to its corresponding NHS ester (6iv). Ester (6iv) was then coupled with the amino terminus of hepta-L-arginine (SEQ ID NO:3), giving the N-Boc protected CsA conjugate (6v). Finally, removal of the Boc protecting group with formic acid afforded the conjugate (6vi) as its octatrifluoroacetate salt after HPLC purification.--

Please replace the paragraph beginning at page 7, line 16, with the following:

--Figure 7 displays inhibition of inflammation in murine contact dermatitis by releasable R7 CsA. Balb/c (6-7 weeks) mice were painted on the abdomen with 100 μl of 0.7% DNFB in acetone olive oil (95:5). Three days later both ears of the animals were restimulated with 0.5% DNFB in acetone. Mice were treated one, five, and twenty hours after restimulation with either vehicle alone, 1% R7 (SEQ ID NO:3) peptide alone, 1% CsA, 1% nonreleasable R7 CsA, 0.01%/0.1% /1.0% releasable R7 CsA, and the fluorinated steroid positive control 0.1% triamcinolone acetonide. Ear inflammation was measured 24 hours after restimulation using a spring loaded caliper. The percent reduction of inflammation was calculated using the following formula (t-n)/(u-n), where t = thickness of the treated ear, n = the thickness of a normal untreated ear, and u = thickness of an inflamed ear without any treatment. N = 20 animals in each group.--

Please replace the paragraph beginning at page 7, line 29, with the following:

--Figure 9 shows a procedure for linking the Cu-DTPA to a transporter (SEQ ID NOS:70-72) through an aminocaproic acid.--

Please replace the paragraph beginning at page 8, line 10, with the following:

--Figure 15A-C shows a reaction scheme for the formation of other C-2' taxol-peptide conjugates (SEQ ID NOS:3, 74 and 75).--

Please replace the paragraph beginning at page 8, line 23, with the following:

--Figure 21 shows the FACS cellular uptake assay of truncated analogs of Tat_{49-57} (Fl-ahx-RKKRRQRRR; SEQ ID NO:8): Tat_{49-56} (Fl-ahx-RKKRRQRR; SEQ ID NO:9), Tat_{49-55}

(Fl-ahx-RKKRRQR; SEQ ID NO:10), Tat_{50-57} (Fl-ahx-KKRRQRRR; SEQ ID NO:11), and Tat_{51-57} (Fl-ahx-KRRQRRR; SEQ ID NO:12). Jurkat cells were incubated with varying concentrations (12.5 μM shown) of peptides for 15 min at 23 °C.--

Please replace the paragraph beginning at page 8, line 28, with the following:

--Figure 22 shows FACS cellular uptake assay of alanine-substituted analogs of Tat_{49-57}: A-49 (Fl-ahx-AKKRRQRRR; SEQ ID NO:13), A-50 (Fl-ahx-RAKRRQRRR; SEQ ID NO:14), A-51 (Fl-ahx-RKARRQRRR; SEQ ID NO:15), A-52 (Fl-ahx-RKKARQRRR; SEQ ID NO:16), A-53 (Fl-ahx-RKKRAQRRR; SEQ ID NO:17), A-54 (Fl-ahx-RKKRRARRR; SEQ ID NO:18), A-55 (Fl-ahx-RKKRRQARR; SEQ ID NO:19), A-56 (Fl-ahx-RKKRRQRAR; SEQ ID NO:20), and A-57 (Fl-ahx-RKKRRQRRA; SEQ ID NO:21). Jurkat cells were incubated with varying concentrations (12.5 μM shown) of peptides for 12 min at 23 °C.--

Please replace the paragraph beginning at page 9, line 3, with the following:

--Figure 23 shows the FACS cellular uptake assay of *d*- and retro-isomers of Tat_{49-57}: *d*-Tat49-57 (Fl-ahx-rkkrrqrrr), Tat57-49 (Fl-ahx-RRRQRRKKR; SEQ ID NO:22), and *d*-Tat57-49 (Fl-ahx-rrrqrrkkr). Jurkat cells were incubated with varying concentrations (12.5 μM shown) of peptides for 15 min at 23 °C.--

Please replace the paragraph beginning at page 9, line 7, with the following:

--Figure 24 shows the FACS cellular uptake of a series of arginine oligomers and Tat_{49-57}: R5 (Fl-ahx-RRRRR; SEQ ID NO:23), R6 (Fl-ahx-RRRRRR; SEQ ID NO:24), R7 (Fl-ahx-RRRRRRR; SEQ ID NO:25), R8 (Fl-ahx-RRRRRRRR; SEQ ID NO:26), R9 (Fl-ahx-RRRRRRRRR; SEQ ID NO:27), r5 (Fl-ahx-rrrrr), r6 (Fl-ahx-rrrrrr), r7 (Fl-ahx-rrrrrrr), r8 (Fl-

ahx-rrrrrrrr), r9 (Fl-ahx-rrrrrrrrr). Jurkat cells were incubated with varying concentrations (12.5 μM shown) of peptides for 4 min at 23 °C.--

Please replace the paragraph beginning at page 9, line 12, with the following:

--Figure 25 displayes the preparation of guanidine-substituted peptoids (SEQ ID NOS:76-80).--

Please replace the paragraph beginning at page 9, line 13, with the following:

--Figure 26 displays the FACS cellular uptake of polyguanidine peptoids (SEQ ID NOS:76, 78 and 80) and *d*-arginine oligomers. Jurkat cells were incubated with varying concentrations (12.5 μM shown) of peptoids and peptides for 4 min at 23 °C.--

Please replace the paragraph beginning at page 9, line 27, with the following:

--Figure 31A and Figure 31B show synthetic schemes for making conjugates in which FK506 is attached to a delivery-enhancing transporter (SEQ ID NOS:81 and 82).--

Please replace the paragraph beginning at page 13, line 15, with the following:

--The term "peptide" as used herein refers to a compound made up of a single chain of D- or L- amino acids or a mixture of D- and L-amino acids joined by peptide bonds. Generally, peptides contain at least two amino acid residues and are less than about 50 amino acids in length. D-amino acids are represented herein by a lower-case one-letter amino acid symbol (*e.g.*, r for D-arginine), whereas L-amino acids are represented by an upper case one-

letter amino acid symbol (*e.g.*, R for L-arginine). Homopolymer peptides are represented by a one-letter amino acid symbol followed by the number of consecutive occurrences of that amino acid in the peptide- (*e.g.*, R7 (SEQ ID NO:3) represents a heptamer that consists of L-arginine residues).--

Please replace the paragraph beginning at page 14, line 25, with the following:

--The delivery-enhancing transporters increase delivery of the conjugate into and across one or more intact epithelial or endothelial tissue layers compared to delivery of the compound in the absence of the delivery-enhancing transporter. The delivery-enhancing transporters can, in some embodiments, increase delivery of the conjugate significantly over that obtained using the tat protein of HIV-1 (Frankel *et al.* (1991) PCT Pub. No. WO 91/09958). Delivery is also increased significantly over the use of shorter fragments of the tat protein containing the tat basic region (residues 49-57 having the sequence RKKRRQRRR; SEQ ID NO:28) (Barsoum *et al.* (1994) WO 94/04686 and Fawell *et al.* (1994) *Proc. Nat'l. Acad. Sci. USA* 91: 664-668). Preferably, delivery obtained using the transporters of the invention is increased more than 2-fold, still more preferably six-fold, still more preferably ten-fold, and still more preferably twenty-fold, over that obtained with tat residues 49-57. In some embodiments, the compositions of the invention do not include tat residues 49-57.--

Please replace the paragraph beginning at page 15, line 6, with the following:

--Similarly, the delivery-enhancing transporters of the invention can provide increased delivery compared to a 16 amino acid peptide-cholesterol conjugate derived from the *Antennapedia* homeodomain that is rapidly internalized by cultured neurons (Brugidou *et al.* (1995) *Biochem. Biophys. Res. Commun.* 214: 685-93). This region, residues 43-58 at minimum, has the amino acid sequence RQIKIWFQNRRMKWKK (SEQ ID NO:29). The *Herpes simplex* protein VP22, like tat and the *Antennapedia* domain, was previously known to enhance transport

into cells, but was not known to enhance transport into and across endothelial and epithelial membranes (Elliot and O'Hare (1997) *Cell* 88: 223-33; Dilber *et al.* (1999) *Gene Ther.* 6: 12-21; Phelan *et al.* (1998) *Nature Biotechnol.* 16: 440-3). In some embodiments, the delivery-enhancing transporters provide significantly increased delivery compared to the *Antennapedia* homeodomain and to the VP22 protein. In some embodiments, the compositions of the invention do not include the *Antennapedia* homeodomain, the VP22 protein or eight contiguous arginines (SEQ ID NO:4).--

Please replace the paragraph beginning at page 19, line 12, with the following:

--In one group of preferred embodiments, the transport moiety has the formula $(ZYZ)_nZ$ (SEQ ID NOS:33-36), wherein each "Y" is independently selected from glycine, β-alanine, γ-amino butyric acid and ε-amino caproic acid, "Z" is preferably L-arginine, and n is preferably an integer ranging from 2 to 5. More preferably, each "Y" is glycine or ε-amino caproic acid and n is 3 (SEQ ID NO:37). Within this group of embodiments, the use of glycine is preferred for those compositions in which the transport moiety is fused or covalently attached directly to a polypeptide biological agent such that the entire composition can be prepared by recombinant methods. For those embodiments in which the transport moiety is to be assembled using, for example, solid phase methods, ε-amino caproic acid is preferred.--

Please replace the paragraph beginning at page 19, line 21, with the following:

--In another group of preferred embodiments, the transport moiety has the formula $(ZY)_nZ$ (SEQ ID NOS:38-44), wherein each "Y" is preferably selected from glycine, β-alanine, γ-amino butyric acid and ε-amino caproic acid, "Z" is preferably L-arginine, and n is preferably an integer ranging from 4 to 10. More preferably, each "Y" is glycine or ε-amino caproic acid and n is 6 (SEQ ID NO:45). As with the above group of specific embodiments, the use of

glycine is preferred for those compositions in which the transport moiety is fused or covalently attached directly to a polypeptide biological agent such that the entire composition can be prepared by recombinant methods. For solution or solid phase construction of the transport moiety, ε-amino caproic acid is preferred.--

Please replace the paragraph beginning at page 19, line 30, with the following:

--In yet another group of preferred embodiments, the transport moiety has the formula $(ZYY)_nZ$ (SEQ ID NOS:46-52), wherein each "Y" is preferably selected from glycine, β-alanine, γ-amino butyric acid and ε-amino caproic acid, "Z" is preferably L-arginine, and n is preferably an integer ranging from 4 to 10. More preferably, each "Y" is glycine or ε-amino caproic acid and n is 6 (SEQ ID NO:53).--

Please replace the paragraph beginning at page 20, line 4, with the following:

--In still another group of preferred embodiments, the transport moiety has the formula $(ZYYY)_nZ$ (SEQ ID NOS:54-60), wherein each "Y" is preferably selected from glycine, β-alanine, γ-amino butyric acid and ε-amino caproic acid, "Z" is preferably L-arginine, and n is preferably an integer ranging from 4 to 10. More preferably, "Y" is glycine and n is 6 (SEQ ID NO:61).--

Please replace the paragraph beginning at page 20, line 16, with the following:

--One of skill in the art will appreciate that the transport moiety can be a polypeptide fragment within a larger polypeptide. For example, the transport moiety can be of the formula $(ZYY)_nZ$ (SEQ ID NOS:46-52) yet have additional amino acids which flank this

moiety (e.g., $X_m(ZYY)_nZ\text{-}X_p$ (SEQ ID NOS:62-68) wherein the subscripts m and p represent integers of zero to about 10 and each X is independently a natural or non-natural amino acid).--

Please replace the paragraph beginning at page 31, line 25, with the following:

--In one approach, the conjugate can include a disulfide linkage, as illustrated in Figure 5A of PCT application US00/23440 (Publication No. WO01/13957)), (*see also*, PCT application US98/10571 (Publication No. WO 9852614)), which shows a conjugate (I) containing a transport polymer T which is linked to a cytotoxic agent, 6-mercaptopurine, by an N-acetyl-protected cysteine group which serves as a linker. Thus, the cytotoxic agent is attached by a disulfide bond to the 6-mercapto group, and the transport polymer is bound to the cysteine carbonyl moiety via an amide linkage. Cleavage of the disulfide bond by reduction or disulfide exchange results in release of the free cytotoxic agent. A method for synthesizing a disulfide-containing conjugate is provided in Example 9A of PCT application US98/10571. The product described therein contains a heptamer of Arg residues (SEQ ID NO:3) which is linked to 6-mercaptopurine by an N-acetyl-Cys-Ala-Ala linker, where the Ala residues are included as an additional spacer to render the disulfide more accessible to thiols and reducing agents for cleavage within a cell. The linker in this example also illustrates the use of amide bonds, which can be cleaved enzymatically within a cell.--

Please replace the paragraph beginning at page 49, line 19, with the following:

--The releasable R7 CsA conjugate was assayed *in vivo* for functional activity using a murine model of contact dermatitis. Treatment with the 1% releasable R7 CSA conjugate resulted in 73.9% ± 4.0 reduction in ear inflammation (Figure 7). No reduction in inflammation was seen in the untreated ear, indicating that the effect seen in the treated ear was local and not systemic. Less inhibition was observed in the ears of mice treated with 0.1 and 0.01% R7-CsA (64.8% ± 4.0 and 40.9% ± 3.3 respectively), demonstrating that the effect was

titratable. Treatment with the fluorinated corticosteroid positive control resulted in reduction in ear swelling (34.1% ± 6.3), but significantly less than that observed for 0.1% releasable R7 CsA (Figure 7). No reduction of inflammation was observed in any of the mice treated with unmodified Cyclosporin A, vehicle alone, R7 (SEQ ID NO:3), or nonreleasable R7 CsA.--

Please replace the paragraph beginning at page 50, line 20, with the following:

--DTPA-aca-R7-CO2H (SEQ ID NO:31) (10 mg, 0.0063 mmol) and copper sulfate (1.6 mg, 0.0063 mmol) were dissolved in water (1 mL). Let gently stir for 18 h and lyophilized to provide product as a white powder (10 mg).--

Please replace the paragraph beginning at page 53, line 24, with the following:

--**General Procedure for Peptide Synthesis**. Tat_{49-57} (RKKRRQRRR; SEQ ID NO:28), truncated and alanine-substituted peptides derived from Tat_{49-57}, $Antennapedia_{43-58}$ (RQIKIWFQNRRMKWKK; SEQ ID NO:29), and homopolymers of arginine (R5-R9; SEQ ID NOS:1-5) and *d*-arginine (r5-r9) were prepared with an automated peptide synthesizer (ABI433) using standard solid-phase Fmoc chemistry (35) with HATU as the peptide coupling reagent. The fluorescein moiety was attached via a aminohexanoic acid spacer by treating a resin-bound peptide (1.0 mmol) with fluorescein isothiocyanate (1.0 mmol) and DIEA (5 mmol) in DMF (10 mL) for 12 h. Cleavage from the resin was achieved using 95:5 TFA/triisopropylsilane. Removal of the solvent in vacuo gave a crude oil which was triturated with cold ether. The crude mixture thus obtained was centrifuged, the ether was removed by decantation, and the resulting orange solid was purified by reverse-phase HPLC (H_2O/CH_3CN in 0.1% TFA). The products were isolated by lyophilization and characterized by electrospray mass spectrometry. Purity of the peptides was >95% as determined by analytical reverse-phase HPLC (H_2O/CH_3CN in 0.1% TFA).--

Please replace the paragraph beginning at page 55, line 10, with the following:

--To determine the structural requirements for the cellular uptake of short arginine-rich peptides, a series of fluorescently-labeled truncated analogues of Tat_{49-57} were synthesized using standard solid-phase chemistry. *See, e.g.*, Atherton, E.*et al.* SOLID-PHASE PEPTIDE SYNTHESIS (IRL: Oxford, Engl. 1989). A fluorescein moiety was attached via an aminohexanoic acid spacer on the amino termini. The ability of these fluorescently labeled peptides to enter Jurkat cells was then analyzed using fluorescent activated cell sorting (FACS). The peptide constructs tested were Tat_{49-57} (Fl-ahx-RKKRRQRRR; SEQ ID NO:8): Tat_{49-56} (Fl-ahx-RKKRRQRR; SEQ ID NO:9), Tat_{49-55} (Fl-ahx-RKKRRQR; SEQ ID NO:10), Tat_{50-57} (Fl-ahx-KKRRQRRR; SEQ ID NO:11), and Tat_{51-57} (Fl-ahx-KRRQRRR; SEQ ID NO:12). Differentiation between cell surface binding and internalization was accomplished throughout by running a parallel set of assays in the presence and absence of sodium azide. Because sodium azide inhibits energy-dependent cellular uptake but not cell surface binding, the difference in fluorescence between the two assays provided the amount of fluorescence resulting from internalization.--

Please replace the paragraph beginning at page 56, line 3, with the following:

--To determine the contribution of individual amino acid residues to cellular uptake, analogs containing alanine substitutions at each site of Tat_{49-57} were synthesized and assayed by FACS analysis (Figure 22). The following constructs were tested: A-49 (Fl-ahx-AKKRRQRRR; SEQ ID NO:13), A-50 (Fl-ahx-RAKRRQRRR; SEQ ID NO:14), A-51 (Fl-ahx-RKARRQRRR; SEQ ID NO:15), A-52 (Fl-ahx-RKKARQRRR; SEQ ID NO:16), A-53 (Fl-ahx-RKKRAQRRR; SEQ ID NO:17), A-54 (Fl-ahx-RKKRRARRR; SEQ ID NO:18), A-55 (Fl-ahx-RKKRRQARR; SEQ ID NO:19), A-56 (Fl-ahx-RKKRRQRAR; SEQ ID NO:20), and A-57 (Fl-ahx-RKKRRQRRA; SEQ ID NO:21). Substitution of the non-charged glutamine residue of Tat_{49-57} with alanine (A-54) resulted in a modest decrease in cellular internalization. On the

other hand, alanine substitution of each of the cationic residues individually produced a 70-90% loss of cellular uptake. In these cases, the replacement of lysine (A-50, A-51) or arginine (A-49, A-52, A-55, A-56, A-57) with alanine had similar effects in reducing uptake.--

Please replace the paragraph beginning at page 56, line 25, with the following:

--These initial results indicated that arginine content is primarily responsible for the cellular uptake of Tat_{49-57}. Furthermore, these results were consistent with our previous results where we demonstrated that short oligomers of arginine were more effective at entering cells then the corresponding short oligomers of lysine, ornithine, and histidine. What had not been established was whether arginine homo-oligomers are more effective than Tat_{49-57}. To address this point, Tat_{49-57} was compared to the *l*-arginine (R5-R9; SEQ ID NOS:1-5) and *d*-arginine (r5-r9) oligomers. Although Tat_{49-57} contains eight cationic residues, its cellular internalization was between that of R6 (SEQ ID NO:2) and R7 (SEQ ID NO:3) (Figure 24) demonstrating that the presence of six arginine residues is the most important factor for cellular uptake. Significantly, conjugates containing 7-9 arginine residues exhibited better uptake than Tat_{49-57}.--

Please replace the paragraph beginning at page 57, line 4, with the following:

--To quantitatively compare the ability of these arginine oligomers and Tat_{49-57} to enter cells, Michaelis-Menton kinetic analyses were performed. The rates of cellular uptake were determined after incubation (3 °C) of the peptides in Jurkat cells for 30, 60, 120, and 240 seconds (Table 1). The resultant K_m values revealed that r9 and R9 (SEQ ID NO:5) entered cells at rates approximately 100-fold and 20-fold faster than Tat_{47-59} respectively. For comparison, $Antennapedia_{43-58}$ was also analyzed and was shown to enter cells approximately 2-fold faster than Tat_{47-59}, but significantly slower than r9 or R9 (SEQ ID NO:5).

Table 1: Michaelis-Menton kinetics: Antennapedia$_{43-58}$ (Fl-ahx-RQIKIWFQNRRMKWKK; SEQ ID NO:30), R9 = SEQ ID NO:5.

peptide	$K_m(\mu M)$	V_{max}
Tat$_{49-57}$	770	0.38
Antennapedia$_{43-58}$	427	0.41
R9	44	0.37
r9	7.6	0.38

--

Please replace the paragraph beginning at page 59, line 27, with the following:

--The cellular uptake of fluorescently labeled polyguanidine *N*-arg5,7,9 (SEQ ID NOS:76, 78 and 80) peptoids was compared to the corresponding *d*-arginine peptides r5,7,9 (similar proteolytic properties) using Jurkat cells and FACS analysis. The amount of fluorescence measured inside the cells with *N*-arg5,7,9 (SEQ ID NOS:76, 78 and 80) was proportional to the number of guanidine residues: *N*-arg9 > *N*-arg7 > *N*-arg5 (SEQ ID NOS:76, 78 and 80) (Figure 26), analogous to that found for r5,7,9. Furthermore, the *N*-arg5,7,9 (SEQ ID NOS:76, 78 and 80) peptoids showed only a slightly lower amount of cellular entry compared to the corresponding peptides, r5,7,9. The results demonstrate that the hydrogen bonding along the peptide backbone of Tat$_{49-57}$ or arginine oligomers is not a required structural element for cellular uptake and oligomeric guanidine-substituted peptoids can be utilized in place of arginine-rich peptides as molecular transporters. The addition of sodium azide inhibited internalization demonstrating that the cellular uptake of peptoids was also energy dependent.--

Please replace the paragraph beginning at page 60, line 9, with the following:

--After establishing that the *N*-arg peptoids efficiently crossed cellular membranes, the effect of side chain length (number of methylenes) on cellular uptake was investigated. For a given number of guanidine residues (5,7,9), cellular uptake was proportional to side chain length. Peptoids with longer side chains exhibited more efficient cellular uptake. A nine-mer peptoid analog with a six-methylene spacer between the guanidine head groups and the backbone (*N*-hxg9) exhibited remarkably higher cellular uptake than the corresponding *d*-arginine oligomer (r9). The relative order of uptake was *N*-hxg9 (6 methylene) > *N*-btg9 (4 methylene) > r9 (3 methylene) > *N*-arg9 (SEQ ID NO:80) (3 methylene) > *N*-etg9 (2 methylene) (Figure 27). Of note, the N-hxg peptoids showed remarkably high cellular uptake, even greater than the corresponding d-arginine oligomers. The cellular uptake of the corresponding heptamers and pentamers also showed the same relative trend. The longer side chains embodied in the *N*-hxg peptoids improved the cellular uptake to such an extent that the amount of internalization was comparable to the corresponding *d*-arginine oligomer containing one more guanidine residue (Figure 28). For example, the *N*-hxg7 peptoid showed comparable cellular uptake to r8.--

Please replace the paragraph beginning at page 61, line 4, with the following:

--The nona-peptide, Tat_{49-57}, has been previously shown to efficiently translocate through plasma membranes. The goal of this research was to determine the structural basis for this effect and use this information to develop simpler and more effective molecular transporters. Toward this end, truncated and alanine substituted derivatives of Tat_{49-57} conjugated to a fluoroscein label was prepared. These derivatives exhibited greatly diminished cellular uptake compared to Tat_{49-57}, indicating that all of the cationic residues of Tat_{49-57} are required for efficient cellular uptake. When compared with our previous studies on short oligomers of cationic oligomers, these findings suggested that an oligomer of arginine might be superior to Tat_{49-57} and certainly more easily and cost effectively prepared. Comparison of short arginine

oligomers with Tat_{49-57} showed that members of the former were indeed more efficiently taken into cells. This was further quantified for the first time ~~bt~~ by Michaelis-Menton kinetics analysis which showed that the R9 (SEQ ID NO:5) and r9 oligomers had Km values 30-fold and 100-fold greater than that found for Tat_{49-57}.--

Please replace the paragraph beginning at page 61, line 17, with the following:

--Given the importance of the guanidino head group and the apparent insensitivity of the oligomer chirality revealed in our peptide studies, we designed and synthesized a novel series of polyguanidine peptoids. The peptoids *N*–arg5,7,9 (SEQ ID NOS: 76, 78 and 80), incorporating the arginine side chain, exhibited comparable cellular uptake to the corresponding *d*-arginine peptides r5,7,9, indicating that the hydrogen bonding along the peptide backbone and backbone chirality are not essential for cellular uptake. This observation is consistent with molecular models of these peptoids, arginine oligomers, and Tat_{49-57}, all of which have a deeply embedded backbone and a guanidinium dominated surface. Molecular models further reveal that these structural characteristics are retained in varying degree in oligomers with different alkyl spacers between the peptoid backbone and guanidino head groups. Accordingly, a series of peptoids incorporating 2- (*N*-etg), 4- (*N*-btg), and 6-atom (*N*-hxg) spacers between the backbone and side chain were prepared and compared for cellular uptake with the *N*-arg peptoids (3-atom spacers) and *d*-arginine oligomers. The length of the side chains had a dramatic affect on cellular entry. The amount of cellular uptake was proportional to the length of the side chain with *N*-hxg > *N*-btg > *N*-arg > *N*-etg. Cellular uptake was improved when the number of alkyl spacer units between the guanidine head group and the backbone was increased. Significantly, *N*–hxg9 was superior to r9, the latter being 100-fold better than Tat_{49-57}. This result led us to prepare peptoid derivatives containing longer octyl spacers (*N*-ocg) between the guanidino groups and the backbone. Issues related to solubility prevented us from testing these compounds.--

Please replace the paragraph beginning at page 64, line 4, with the following:

--A solution of the above hydrazone (3) (0.025g, 24.7 μmol), transporter (1x, $Bacar_9CCONH_2.9TFA$, $Bacar_7CCONH_2.7TFA$, $BacaCCONH_2$, $NH_2r_7CCONH_2.8TFA$, $NH_2R_7CCONH_2.8TFA$ (SEQ ID NO:32)) and diisopropylethylamine (1x) in anhydrous dimethylformamide (1mL) were stirred under nitrogen at room temperature for 36h when TLC indicated the complete disappearance of the starting hydrazone. Solvent was evaporated from the reaction mixture and the residue purified by reverse phase HPLC using trifluoroacetic acid buffered water and acetonitrile.--

Please replace the paragraph beginning at page 64, line 11, with the following:

--Yields of conjugates with various transporters:

Conjugate with $Bacar_9CCONH_2.9TFA$ (4) – 73%

$Bacar_7CCONH_2.7TFA$ (5) – 50%

$BacaCCONH_2$ (6) – 52.9%

$NH_2r_7CCONH_2.8TFA$ (7) – 43.8%

$NH_2R_7CCONH_2.8TFA$ (SEQ ID NO:32) (8) – 62.8%--

Please replace the paragraph beginning at page 65, line 4, with the following:

--In this example, cyclosporin is converted to its α-chloroacetate ester using chloroacetic anhydride to provide **6i** (see Figure 6). The ester **6i** is then treated with benzylamine to provide **6ii**. Reaction of the amine with Boc-protected iminodiacetic acid anhydride provides the acid **6iii** which is then converted to an activated ester (**6iv**) with N-hydroxy succinimide. Coupling of **6iv** with L-Arginine heptamer (SEQ ID NO:3) provides the BOC-protected conjugate **6v**, which can be converted to conjugate **6vi** by removal of the BOC protecting group according to established methods.--

Please replace the paragraph beginning at page 65, line 11, with the following:

--Transport moieties having arginine groups separated by, for example, glycine, ϵ-aminocaproic acid, or γ-aminobutyric acid can be used in place of the arginine heptamer (SEQ ID NO:3) in this and in the following examples that show oligoarginine transport groups.--

Please replace the paragraph beginning at page 74, line 13, with the following:

--A solution of the chloroacetic ester of hydrocortisone (0.0137 mmol), a transporter containing a cysteine residue (0.0137) and diisopropylethylamine (DIEA) (0.0274 mmol) in dimethylformamide (DMF) (1 mL) was stirred at room temperature for 18 h (Figure 11). The material was purified via reverse-phase HPLC using a water/acetonitrile gradient and lyophilized to provide a white powder.

r5 conjugate- 12 mg obtained (29% isolated yield)

r7 conjugate- 22 mg obtained (55% isolated yield)

R7 conjugate (SEQ ID NO:73)- 13 mg obtained (33% isolated yield).--

Please replace the paragraph beginning at page 77, line 1, with the following:

--The resultant chloroacetyl ester was dissolved in dry N, N-dimethylformamide under a nitrogen atmosphere. To the solution was added Hunig's base (1 eq) and AcHN-C-aca-R8-CONH2*8 HCl (SEQ ID NO:69) with rapid stirring. The reaction was allowed to proceed until TLC analysis indicated that all of the starting material had been consumed (ca 2 hours). The reaction was halted by removal of the solvent under reduced pressure. The residue was purified by RP-HPLC to provide the desired acyclovir conjugate.--

Please insert the accompanying paper copy of the Sequence Listing, page numbers 1 to 42, at the end of the application.